GeneDx
207 Perry Parkway
Gaithersburg, MD 20877
Phone: 301-519-2100
Fax: 301-519-2892
E-mail: genedx@genedx.com
www.genedx.com

Test Information Sheet

STAT3 and DOCK8 Genes in Hyper IgE Syndrome

Also known as: Hyper-IgE Recurrent Infection Syndrome; Job's Syndrome; HIES; DOCK8 Immunodeficiency Syndrome (DIDS); AR-HIES (autosomal recessive HIES) or AD-HIES (autosomal dominant HIES).

Mendelian Inheritance in Man Number:

STAT3	Dominant	147060	Hyper-IgE recurrent infection syndrome, autosomal dominant
		102582	STAT3 (Signal Transducer and Activator of Transcription 3)
DOCK8	Recessive	243700	Hyper-IgE recurrent infection syndrome, autosomal recessive
		611432	DOCK8 (Dedicator of Cytokinesis 8)

***Clinical features*:**

Patients with **STAT3-associated Hyper-IgE** Syndrome have lifelong eczema, eosinophilia, and recurrent staphylococcal skin abscesses (recalling the infliction of the biblical character Job). The abscesses are "cold", i.e. with remarkably little inflammatory response. Serum IgE levels are characteristically at least 10-fold elevated. Patients are prone to cyst-forming pneumonia (typically staph, hemophilus or pneumococcus) and mucocutaneous candidiasis. The face may be coarse and asymmetric. Non-traumatic fractures and scoliosis are typical, and dental deciduation is delayed. Other features reported include hyperextensibility, coronary artery aneurysms, brain lesions, craniosynostosis, and Chiari malformations. HIES with dominant inheritance can be considered in isolated cases or when parent and child are affected. **DOCK8-associated HIES** is similar, but without the skeletal and connective tissue findings. HIES with recessive inheritance can be considered in isolated cases or when siblings, but not parents are affected, especially, but not exclusively, when some degree of parental consanguinity is possible.

***Reasons for referral*:**

Confirmation of a clinical diagnosis; genetic counseling; carrier testing for DOCK8 mutations; prenatal diagnosis in a family with previously identified mutations.

***Test Method*:**

STAT3 is analyzed for small sequence mutations in probands (index cases) by bi-directional sequencing of exons and splice sites, offered in two tiers. Tier 1 includes exons 12-16, 20 and 21 (covering amino acids 370-488 and 583-700), while Tier 2 includes the remaining 17 exons. DOCK8 is analyzed for gross deletions by the ExonArrayDx test, an exon-level microarray CGH (complete genome hybridization). After mutation identification, subsequent testing of family members is provided for STAT3 as a targeted test using sequencing, restriction fragment analysis or other appropriate method, and for DOCK8 using the ExonArrayDx test or a targeted test for a gross deletion of a specific exon.

Test Sensitivity:

STAT3: The vast majority of mutations in STAT3 are found in exons 13-16, 20 and 21, including extreme hotspots in exons 13 and 21[1,2]. Analysis of those 6 exons plus exon 12 is expected to detect the mutations in 95% of STAT3-associated HIES patients, including a cluster in IVS11 and IVS12 flanking exon 12[3]. Sequencing of the remaining exons will detect all other small sequence changes, but would not detect gross deletions of whole exons. To date, only one such patient has been described[4].

DOCK8: Mutations in DOCK8 include both small sequence changes and gross deletions of one or more exons[5,6]. Sequencing of the 47 exons of DOCK8 is not available at this time, but testing for gross deletions, accounting for 60% of the observed mutations in this gene, is offered for all exons.

Mutation spectrum:

STAT3 mutations in AD-HIES patients almost always are of the type that are readily detected by sequencing[1,2,3,4]. They are small amino acid deletions, insertions, or substitutions, predominantly located in the DNA-binding domain (exons 10-16, of which exons 12-16 are studied) or SH2 domain (exons 20 and 21). In contrast, over half of the DOCK8 mutations observed have been gross deletion of one or more exons[5,6].

Specimen Requirements and Shipping/Handling:

- *Blood* - A single tube with 1-5 mL whole blood in EDTA. Ship overnight at ambient temperature, using a cool pack in hot weather. Specimens may be refrigerated for 7 days prior to shipping.
- *Buccal Brushes* - **Limited to testing of relatives for a known STAT3 mutation only**. Not available for children under 6 months of age. Request a GeneDx buccal kit (others not accepted). Submit by mail.
- *Prenatal Diagnosis:* 10 mL amniotic fluid, 5 mg CVS, or 2 T25 flasks. Ship overnight at ambient temperature, using a cool pack in hot weather. Call to discuss requirements for parental blood. Keep backup cultures.

Required Forms:

Sample Submission (Requisition) Form – complete all pages
Payment Options Form or Institutional Billing Instructions

Prices and Turn-Around Time - *Fees are subject to change without notice:*

Test #312: Sequencing of 7 selected STAT3 exons in a new patient = $890; Approx. 5 weeks
Test# 3122: Sequencing 17 remaining STAT3 exons, reflex or add-on = $2060; Approx. 6 weeks
Test# 906: ExonArrayDx deletion/duplication analysis, all DOCK8 exons = $500; Approx. 4 weeks
Test #9011: Sequencing of a relative for one known mutation* = $350; Approx. 3 weeks
Test #902: Prenatal diagnosis for a specific known mutation* = $2000; Approx. 2 weeks

*Please see our website for CPT codes/prices for carrier and prenatal testing: http://www.genedx.com

CPT codes for mutation detection in a new patient - *All codes and units apply:*

CPT Codes	#312 Sequencing of STAT3 selected exons	# 3122 Sequencing of STAT3 remaining exons	# 906, ExonArrayDx del/dup test of DOCK8, all exons
83891	6 units	17 units	2 units
83896	N/A	N/A	1 unit
83898	12 units	34 units	N/A
83894	6 units	17 units	N/A
83904	12 units	34 units	N/A
83892	2 units	3 units	N/A
83912	2 units	4 units	N/A
Price	**$ 890**	**$ 2060**	**$500**

Possible ICD9 Codes that may apply to some patients with this diagnosis:

288.1 - Job's syndrome or chronic granulomatous disease; 481 - Pneumococcal pneumonia; 482.x - Other pneumonia; 513.0 - Abscess of lung; 680.x - Boil

References:

1. Minegishi Y et al., Dominant-negative mutations in the DNA-binding domain of STAT3 cause hyper-IgE syndrome, Nature 448:1058-1062, 2007
2. Holland SM et al., STAT3 mutations in the Hyper-IgE syndrome, NEJM 357:1608-1619, 2007.
3. Renner ED, et al, Autosomal recessive hyperimmunoglobulin E syndrome: a distinct disease entity. J. Pediatrics 144:93-99, 2004.
4. Schimke, LF et al, Diagnostic approaches to the hyper-IgE syndromes: immunologic and clinical key findings to differentiate hyper-IgE syndromes from atopic dermatitis, J Allergy Clin Immunol, 126:611-617, 2010.
5. Zhang Q, et al. Combined immunodeficiency associated with DOCK8 mutations, NEJM 361:2046-2055, 2009.
6. Engelhardt, KR, et al., Large deletions and point mutations involving the dedicator of cytokinesis 8 (DOCK8) in the autosomal-recessive form of hyper-IgE syndrome, J Allergy Clin Immunol 124:1289-1302, 2009.

GeneDx
DNA DIAGNOSTIC EXPERTS
WHERE *Rare* is *Common*

Sample Submission Form

Testing Services for Rare Mendelian Disorders

For autism, cardiology, array CGH, FISH, mitochondrial testing, or prenatal testing please use specific submission forms available at www.genedx.com

Patient information

First name _____ Last name _____

Gender: ❒ Female ❒ Male ❒ Unknown ❒ Fetus of

Date of birth (mm/dd/yy) _____

Mailing address _____

City _____ State _____ Zip Code _____

Home phone _____ Work Phone _____

-Sample Information

Medical record # _____ Specimen ID # _____

Date sample obtained (mm/dd/yy) _____

Sample Type *(Note: only ONE specimen is required for multiple tests)*

❒ blood in EDTA (purple top - one tube of 1-5ml)
❒ buccal brushes (must be GeneDx kits)
❒ skin punch biopsy, size _____mm
❒ DNA _____ (source?) _____ (ug/ml)
❒ fetal sample _____ (tissue source?)

If other samples submitted

Relationship to patient _____ Name _____ Sample type _____

Relationship to patient _____ Name _____ Sample type _____

Reporting Address

Physician _____ CGC _____

Facility Name _____

❒ CareEvolve account _____ CE account #

Address _____

Phone _____ Fax (important) _____

Beeper _____ Email _____

Second Report Address (if applicable)

Physician _____ CGC _____

Address _____

Phone _____ Fax (important) _____

Beeper _____ Email _____

Test requested

Write gene/disease name below or check box on pages 2-6

_____

_____

❒ **Testing for known mutation (Go to page 2):**

Mutation: _____ GeneDx ID of relative _____

If expedited testing is requested, please indicate reason:

❒ Pregnancy (gestational age _____ weeks ❒ Transplantation
❒ Other _____

Reason for testing - please complete (required):

❒ Diagnosis ❒ Presymptomatic diagnosis ❒ Carrier testing
❒ Prenatal ❒ Other _____
❒ Positive control sample (no report issued) for patient/relative:

GeneDx ID _____ First name _____ Last name _____

For metabolic disorders - please complete:

Enzyme assay positive ❒ Yes ❒ No ❒ Not done
Newborn screen positive ❒ Yes ❒ No

Clinical diagnosis and family history

Please provide relevant information below including the names or GeneDx ID# of any relatives previously tested.

Patient's karyotype if relevant _____

Ordering Checklist

❒ Sample submission form (pages 1-6) ❒ Completed payment form (page 7)
❒ Informed consent (if appropriate) ❒ Specimen tube labeled

For office use only:

Testing Services for Rare Mendelian Disorders

For autism, cardiology, array CGH, or FISH, mitochondrial testing, or prenatal testing please use specific submission forms available at www.genedx.com

Please check appropriate boxes below and fax only the sheets necessary

Special services (complete box to the right)

Mutation-specific testing
- ❑ 9011 One known familial mutation
- ❑ 9012 Two known familial mutations

Prenatal testing
- ❑ 902 Known familial mutation(s)
- ❑ 9023 Maternal cell contamination studies only

Mutation confirmations
- ❑ 9001 One known mutation identified in a research lab
- ❑ 9002 Two known mutations identified in a research lab

Custom deletion/duplication testing (CopyDx)
- ❑ 903 One gene or locus

Deletion/duplication testing for a gene on the current menu
- ❑ 904 One gene or locus

Follow-up testing for known familial deletion or duplication
- ❑ 905 One gene or locus

DNA extraction only
- ❑ 909 One sample

ExonArrayDx: Exon-level gene-specific deletion/duplication testing by aCGH
- ❑ Deletion/duplication testing for_____

For special services please provide the information below

Known mutation in relative (please send copy of report):

❑ Relative tested at GeneDx GeneDx ID/Name of relative_____

❑ Relative tested at another lab **(Positive control required)**

❑ Positive control Included

Required Information:

_____
Gene or locus

_____
Mutation(s)

_____
Relationship to patient

Fill in genes, disorders, or gene panel to be tested; see ExonArrayDx gene lists at http://www.genedx.com.

FISH testing is available for many of the disorders listed below. Please refer to and use the Molecular Cytogenetics submission form downloadable at www.genedx.com

Mitochondrial testing is available for many disorders. Please refer to and use the Mitochondiral submission form downloadable at www.genedx.com

TEST CODE TEST NAME

Alagille Syndrome (JAG1)
- ❑ 1001 Tier 1 JAG1 sequencing and deletion/duplication testing
- ❑ 1002 Tier 2 JAG1 sequencing, if Tier1 negative
- ❑ 1004 JAG1 full sequencing and deletion/duplication testing NOW

Autism spectrum disorders
Autism/macrocephaly syndrome (PTEN)
- ❑ 195 PTEN sequencing and deletion/duplication testing

Rett syndrome / Atypical Rett syndrome (MECP2)
- ❑ 3041 MECP2 sequencing
- ❑ 906 MECP2 deletion/duplication testing if sequencing is negative

X-linked infantile spasm / Atypical Rett (CDKL5/STK9)
- ❑ 3051 CDKL5 sequencing
- ❑ 906 CDKL5 deletion/duplication testing if sequencing is negative

Bone marrow failure syndromes
- ❑ 104 Congenital amegakaryocytic thrombocytopenia (MPL)
- ❑ 505 X-linked Thrombocytopenia –or– X-linked Neutropenia (WAS)
- ❑ 105 Severe congenital neutropenia, autosomal dominant (ELANE aka ELA2)
- ❑ 303 Severe congenital neutropenia, autosomal recessive (HAX1)

Diamond-Blackfan anemia (specify concurrent or reflex ordering)
- ❑ 1061 RPS19 sequencing
- ❑ 361 RPL5 sequencing
- ❑ 362 RPL11 sequencing
- ❑ 906 RPS19 deletion/duplication testing

Dyskeratosis congenita (specify concurrent or reflex ordering)
- ❑ 108 DKC1 gene, X-linked, sequencing
- ❑ 414 TINF2 gene, exon 6 only, autosomal dominant, sequencing
- ❑ 107 TERC gene, autosomal dominant, sequencing
- ❑ 906 TERC gene, del/dup testing
- ❑ 906 DKC1 gene, del/dup testing in females

- ❑ 109 Shwachman-Diamond Syndrome (SBDS)

Congenital ichthyoses
- ❑ 114 Chanarin-Dorfman syndrome (ABHD5/CGI-58)

Congenital recessive ichthyosis (erythrodermic)
- ❑ 1151 ALOX12B ❑ 1152 ALOXE3 ❑ 1153 ICHTHYIN

Epidermolytic Ichthyosis (Epidermolytic Hyperkeratosis) (KRT1, KRT2, KRT10)
- ❑ 1181 KRT1, KRT10 mutation hotspots
- ❑ 1182 KRT1 sequencing ❑ 1183 KRT10 sequencing
- ❑ 122 KRT2 mutations hotspot

- ❑ 119 Erythrokeratodermia variabilis (GJB3, GJB4)
- ❑ 120 Harlequin ichthyosis (ABCA12)
- ❑ 123 Ichthyosis vulgaris (FLG common mutations)
- ❑ 124 Keratitis-ichthyosis-deafness (KID) (GJB2; connexin26)
- ❑ 125 Lamellar ichthyosis (TGM1)
- ❑ 126 Lamellar ichthyosis type 2 (N.African) (ABCA12 hotspots)
- ❑ 127 Netherton syndrome (SPINK5)
- ❑ 128 Sjögren-Larsson syndrome (FALDH/ALDH3A2)

Disorders involving bones and limbs
Campomelic dysplasia
- ❑ 338 SOX9 sequencing
- ❑ 906 SOX9 deletion/duplication testing if sequencing is negative

- ❑ 285 Cherubism (SH3BP2)

Duane-Radial-Ray syndrome (DRRS; SALL4) †
- ❑ 262 SALL4 sequencing and deletion/duplication testing
- ❑ 408 Prenatal SALL4 test based on fetal ultrasound abnormalities

Grieg Cephalopolysyndactyly syndrome
- ❑ 472 GLI3 sequence (exons 2-15) and deletion/duplication analysis

Hereditary Multiple Exostosis (EXT1/EXT2)
- ❑ 1811 EXT1 sequencing and EXT1/EXT2 deletion/duplication testing
- ❑ 1812 EXT2 sequencing
- ❑ 1813 EXT1+EXT2 sequencing and deletion/duplication testing NOW

Holt-Oram syndrome (TBX5) †
- ❑ 2361 TBX5 sequencing
- ❑ 906 TBX5 deletion/duplication testing if sequencing is negative
- ❑ 2363 Prenatal TBX5 test based on ultrasound abnormalities

- ❑ 3272 Osteoporosis-pseudoglioma syndrome (LRP5)
- ❑ 3272 Osteopetrosis type 1, autosomal dominant (LRP5)
- ❑ 248 Popliteal pterygium syndrome (IRF6, exon 4 only)

Pallister Hall Syndrome
- ❑ 4711 Tier 1 GLI3 sequence analysis of exons 13-15
- ❑ 4712 Tier 2 GLI3 sequence analysis of remaining exons (2-12) and del/dup analysis

Pseudoachondroplasia/multiple epiphyseal dysplasia (COMP) †
- ❑ 249 COMP sequencing
- ❑ 906 COMP deletion/duplication testing if sequencing is negative

Specimen Requirements ALL tests offered by GeneDx can be performed with whole blood specimen. As an alternative to blood, buccal specimen collection kits (supplied by GeneDx) can be used for many tests. Some exceptions are tests marked with "†" and any deletion/duplication, microarray, and non-conventional sequencing tests.

Please check appropriate boxes below and fax only the sheets necessary

TEST CODE TEST NAME

Townes-Brocks syndrome (SALL1) †
- ❑ 2521 SALL1 sequencing
- ❑ 906 SALL1 deletion/duplication testing if sequencing is negative
- ❑ 2523 Prenatal SALL1 test based on fetal ultrasound abnormalities

Disorders of the immune system

- ❑ 154 Agammaglobulinemia, X-linked, BTK sequencing and deletion/duplication testing

Autoimmune lymphoproliferative syndrome (ALPS)
- ❑ 138 ALPS1A (TNFRSF6) sequencing
- ❑ 2611 ALPS2A (CASP10) sequencing ❑ 2612 ALPS2B (CASP8) sequencing

Autoimmune polyendocrinopathy/APECED (AIRE)
- ❑ 1391 Tier 1 AIRE sequencing
- ❑ 1392 Tier 2 AIRE sequencing, if Tier 1 negative
- ❑ 1393 AIRE full gene sequencing NOW

Chronic granulomatous disease (CGD) (specify concurrent or reflex ordering)
- ❑ 1434 CYBB sequencing (X-linked)
- ❑ 1435 NCF1 exon 2 only (recessive)
- ❑ 1431 Above two at the same time (aka Tier 1)
- ❑ 1436 CYBA sequencing (recessive)
- ❑ 1437 NCF2 sequencing (recessive)
- ❑ 1433 Above two at the same time (aka Tier 2)
- ❑ 906 CYBB (X-linked) del/dup test for females

Hyper-IgE syndrome (specify concurrent or reflex ordering)
- ❑ 312 STAT3 sequence, selected exons (dominant)
- ❑ 3122 STAT3 sequence, remaining exons (dominant)
- ❑ 906 DOCK8 deletion/duplication testing (recessive)

- ❑ 318 Hyper-IgM syndrome, AICDA sequencing
- ❑ 301 IRAK4 deficiency, IRAK4 sequencing
- ❑ 146 Leukocyte adhesion deficiency, ITGB2 sequencing

Severe combined immune deficiency (SCID)
- ❑ 492 X-linked SCID, IL2RG sequencing
- ❑ 352 Adenosine deaminase deficiency, ADA sequencing
- ❑ 145 JAK3 deficiency, JAK3 sequencing
- ❑ 147 RAG1 and RAG2 deficiency (include Omenn Syndrome) sequencing
- ❑ 302 IL7R deficiency, IL7R sequencing

SCID with radiation sensitivity (ARTEMIS/DCLRE1C)
- ❑ 1501 DCLRE1C full gene sequencing and deletion/duplication testing
- ❑ 1502 DCLRE1C exon 8 only for Athabascan Indians

Wiskott Aldrich Syndrome (X-linked)
- ❑ 505 WAS gene sequencing
- ❑ 906 WAS gene deletion/duplication testing for females

Ectodermal dysplasia syndromes

X-linked hypohidrotic ED (EDA aka ED1) †
- ❑ 1601 EDA sequencing (males)
- ❑ 1601E EDA sequencing and deletion/duplication testing (females)

- ❑ 373 Autosomal recessive/dominant ED/Odonto-onycho-dermal dysplasia, Schöpf-Schulz-Passarge Syndrome (WNT10A)
- ❑ 156 Autosomal recessive/dominant hypohidrotic ED (EDAR)
- ❑ 157 Clouston syndrome, GJB6, connexin30 sequencing
- ❑ 306 Focal dermal hypoplasia/Goltz syndrome (PORCN)
- ❑ 158 Ectrodactyly-ED-clefting, Hay-Wells syndrome TP63 (p63) sequencing
- ❑ 407 Prenatal p63 test based on ultrasound abnormalities
- ❑ 2863 Hypohidrotic ED with immunodeficiency, IKBKG/NEMO sequencing

Epidermolysis bullosa

- ❑ 162 Epidermolysis bullosa, dystrophic (COL7A1)

Epidermolysis bullosa, simplex (KRT5, KRT14 mutation hotspots; PLEC1)
- ❑ 168 KRT5/KRT14 mutation hotspots
- ❑ 3481 PLEC1 tier 1 ❑ 3482 PLEC1 tier 2

Epidermolysis bullosa, junctional (Herlitz / non-Herlitz)
- ❑ 1631 Tier 1 (hotspots LAMB3, LAMC2, LAMA3)
- ❑ 1632 LAMB3 full sequencing
- ❑ 1633 LAMC2 full sequencing
- ❑ 1634 LAMA3 full sequencing
- ❑ 1636 GABEB/non-Herlitz form (COL17A1)

Epidermolysis bullosa with muscular dystrophy (PLEC1)
- ❑ 3481 PLEC1 Tier 1 sequencing
- ❑ 3482 PLEC1 Tier 2 sequencing

TEST CODE TEST NAME

Epidermolysis bullosa with pyloric atresia (JEB-PA)
- ❑ 1641 ITGB4 sequencing ❑ 1642 ITGA6 sequencing
- ❑ 3481 PLEC1 tier 1 ❑ 3482 PLEC1 tier 2

Eye Disorders

Aniridia, other developmental eye disorders (PAX6)
- ❑ 491 PAX6 sequencing and deletion/duplication PAX6/DCDC1/ELP4/WT1

Anophthalmia, Microphthalmia (SOX2, OTX2, VSX2)
- ❑ 132 SOX2 sequencing
- ❑ 906 SOX2 deletion/duplication testing if sequencing is negative
- ❑ 343 OTX2 sequencing
- ❑ 906 OTX2 deletion/duplication testing if sequencing is negative
- ❑ 344 VSX2 sequencing
- ❑ 428 Prenatal SOX2, OTX2, VSX2 test based on ultrasound abnormalities

Axenfeld-Rieger syndrome † (PITX2, FOXC1)
- ❑ 1341 PITX2 sequencing
- ❑ 906 PITX2 deletion/duplication testing if sequencing is negative
- ❑ 1342 FOXC1 sequencing
- ❑ 906 FOXC1 deletion/duplication testing if sequencing is negative

- ❑ 403 BEST1 related disorders (BEST1, VMD2)

Bothnia retinal dystrophy
- ❑ 4242 RLBP1 BRD: R234W mutation only

Choroideremia (CHM)
- ❑ 296 CHM sequencing
- ❑ 906 CHM del/dup testing if sequencing is negative

Cone and cone-rod dystrophies
- ❑ 379 AIPL1 sequencing
- ❑ 468 Cone rod dystrophy panel: ABCA4, PRPH2 (RDS)
- ❑ 353 CRX sequencing
- ❑ 476 GUCA1A sequencing
- ❑ 467 GUCY2D exon 13 only

Congenital nystagmus, X-linked (FRMD7)
- ❑ 432 FRMD7 sequencing
- ❑ 906 FRMD7 deletion/duplication testing in females if sequencing is negative

Congenital stationary night blindess, autosomal dominant
- ❑ 298 RHO sequencing

Congenital stationary night blindess, autosomal recessive
- ❑ 489 TRPM1 sequencing
- ❑ 427 RDH5 sequencing

Congenital stationary night blindess, X-linked
- ❑ 431 NYX sequencing

Familial exudative vitreoretinopathy (FZD4, LRP5, NDP, TSPAN12)
- ❑ 3271 FZD4 sequencing
- ❑ 3272 LRP5 sequencing
- ❑ 906 LRP5 deletion/duplication testing if sequencing negative
- ❑ 3273 NDP sequencing in males
- ❑ 3274 NDP sequencing and deletion/duplication testing in females
- ❑ 3275 TSPAN12 sequencing

Fundus albipunctatus
- ❑ 427 RDH5 sequencing
- ❑ 4241 RLBP1 sequencing

Glaucoma (CYP1B1, MYOC, OPTN)

Primary congenital glaucoma
- ❑ 330 CYP1B1 sequencing

Primary open-angle glaucoma / juvenile open-angle glaucoma
- ❑ 329 MYOC sequencing

Primary open-angle glaucoma / Normal tension glaucoma
- ❑ 346 OPTN sequencing

Leber congenital amaurosis, autosomal recessive. Tiered panel (reflex testing)
- ❑ 2980 Tier 1: Common mutations (CEP290, GUCY2D, AIPL1, CRB1, RPE65)
- ❑ 2981 Tier 2: CRB1 exons 1-6, 8, 10-12 only
- ❑ 2982 Tier 3: RPE65 exons 2-3, 6-7, 11-14 only
- ❑ 2983 Tier 4: GUCY2D exons 3-11, 14, 16-19 only
- ❑ 2984 Tier 5: AIPL1 exons 1, 3, 5
- ❑ 2985 Tier 6: RPGRIP1 (entire gene)

Leber congenital amaurosis, autosomal dominant. Tiered panel (reflex testing)
- ❑ 412 Tier 1: IMPDH1 full gene sequencing
- ❑ 353 Tier 2: CRX full gene sequencing

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Please check appropriate boxes and fax only the sheets necessary

TEST CODE TEST NAME

Leber congenital amaurosis, comprehensive panel (CEP290, GUCY2D, CRB1, RPE65, AIPL1, IMPDHI, CRX, RPGRIP1)
- ❑ 376 CEP290 gene: IVS26+1655A>G mutation only
- ❑ 377 Entire GUCY2D gene NOW
- ❑ 378 Entire CRB1 gene NOW
- ❑ 345 Entire RPE65 gene NOW
- ❑ 379 Entire AIPL1 gene NOW
- ❑ 412 Entire IMPDH1 gene NOW
- ❑ 353 Entire CRX gene NOW
- ❑ 2985 Entire RPGRIP1 gene NOW

Lenz microphthalmia syndrome (BCOR)
- ❑ 370 BCOR LMS: P85L mutation only

Newfoundland rod-cone dystrophy
- ❑ 4243 RLBP1 NFRCD: IVS4+2 T>C and c.141G>A (K47K) mutations only

Norrie disease (NDP)
- ❑ 3273 NDP sequencing in males
- ❑ 3274 NDP sequencing and deletion/duplication testing in females

Oculofaciocardiodental syndrome (BCOR; females only)
- ❑ 3691 BCOR Tier 1: mutation hotspots and deletion/duplication testing
- ❑ 3692 BCOR Tier 2: Rest of gene sequencing if Tier 1 is negative
- ❑ 3693 BCOR full gene sequencing and deletion/duplication testing NOW

Progressive external ophthalmoplegia
- ❑ 394 POLG sequencing

Retinitis pigmentosa, autosomal dominant, tiered panel (reflex testing)
- ❑ 2971 Tier 1: Common mutations (IMPDH1, RP1, PRPF8, PRPH2 (RDS) full, RHO full)
- ❑ 2975 Tier 2: PRPF31 gene sequencing and deletion/duplication testing
- ❑ 2974 Tier 3: IMPDH1 rest of gene sequencing

Retinitis pigmentosa, autosomal dominant, additional genes
- ❑ 2973 Retinitis pigmentosa, autosomal dominant, PRPF3 gene sequencing
- ❑ 353 Retinitis pigmentosa, autosomal dominant CRX sequencing
- ❑ 403 Retinitis pigmentosa, autosomal dominant BEST1 sequencing

Retinitis pigmentosa, autosomal dominant, individual genes
- ❑ 412 Retinitis pigmentosa, autosomal dominant IMPDH1 sequencing
- ❑ 295 Retinitis pigmentosa, autosomal dominant RP1 sequencing
- ❑ 298 Retinitis pigmentosa, autosomal dominant RHO sequencing
- ❑ 299 Retinitis pigmentosa, autosomal dom. PRPH2 (RDS) sequencing
- ❑ 300 Retinitis pigmentosa, autosomal dominant PRPF8 sequencing

Retinitis pigmentosa panel (7 genes), autosomal recessive/sporadic RP
- ❑ 368 USH2A, EYS, ABCA4, PDE6A, PDE6B, RPE65, CRB1 sequencing
- ❑ 908 Autosomal recessive RP panel - deletion/duplication testing
- ❑ 417 CNGA1 sequencing

Retinitis pigmentosa, X-linked
- ❑ 326 RP2 sequencing
- ❑ 906 RP2 deletion/duplication testing if sequencing negative, females

Retinitis punctata albescens
- ❑ 4241 RLBP1 sequencing

❑ 474 Septo-optic dysplasia (HESX1)

Stargardt panel: Stargardt disease, fundus flavimaculatus, Stargardt-like macular dystrophy, other maculopathies
- ❑ 466 ABCA4, PRPH2 (RDS), and ELOVL4

Stargardt-like macular dystrophy, autosomal dominant
- ❑ 2990 Tier 1: ELOVL4 mutations hot spot
- ❑ 2991 Tier 2: ELOVL4 remaining exons

X-linked juvenile retinoschisis
- ❑ 2571 RS1 sequencing
- ❑ 906 RS1 del/dup testing if sequencing is negative, females only

Familial hyperparathyroid syndromes/Endocrine neoplasias

- ❑ 169 Autosomal dominant hypocalcemia (CASR)
- ❑ 170 Familial hypocalciuric hypercalcemia (CASR)
- ❑ 171 Familial isolated hypoparathyroidism (CASR)

Hyperparathyroidism-jaw tumor syndrome or parathyroid carcinoma or familial isolated hyperparathyroidism (HRPT2)
- ❑ 1731 Tier 1 HRPT2 sequencing
- ❑ 1732 Tier 2, if Tier1negative
- ❑ 173 HRPT2 full gene sequencing NOW

Multiple Endocrine Neoplasia Type 1 (MEN1, Menin)
- ❑ 176 MEN1 sequencing
- ❑ 904 MEN1 deletion/duplication testing if sequencing is negative

❑ 177 Multiple endocrine neoplasia Type 2A or familial medullary thyroid carcinoma, RET sequencing

❑ 178 Multiple endocrine neoplasia type 2B, RET sequencing

❑ 180 Neonatal severe primary hyperparathyroidism, CASR sequencing

Hereditary rickets

- ❑ 184 Autosomal dominant hypophosphataemia (FGF23)
- ❑ 185 Autosomal recessive vitamin D-dependent rickets (CYP27B1)
- ❑ 314 Autosomal recessive hypophosphatemic rickets (DMP1)

X-linked dominant hypophosphatemia (PHEX)
- ❑ 1861 PHEX sequencing in males
- ❑ 1861E PHEX sequencing and deletion/duplication testing in females

Inborn errors of metabolism

- ❑ 508 3-Hydroxyacyl-CoA dehydrogenase deficiency (HADH)
- ❑ 380 6-pyruvoyl--tetrahydropterin synthase deficiency (PTS)
- ❑ 354 ß-ketothiolase deficiency (ACAT1)
- ❑ 465 Arginase deficiency (ARG1)
- ❑ 426 Argininosuccinic Aciduria (ASL)
- ❑ 294 Biotinidase deficiency (BTD)
- ❑ 429 Carnitine-Acylcarnitine Translocase Deficiency (SLC25A20)
- ❑ 425 Carnitine palmitoyltransferase IA deficiency (CPT1A)
- ❑ 334 Carnitine palmitoyltransferase deficiency type II (CPT2)
- ❑ 500 Citrin Deficiency (SLC25A13)
- ❑ 382 Classic Citrullinemia (ASS1)
- ❑ 274 Cobalamin C deficiency (MMACHC)
- ❑ 490 Dihydrolipoamide Dehydrogenase Deficiency (DLD)
- ❑ 381 Dihydropteridine reductase (DHPR) deficiency (QDPR)
- ❑ 411 Ethylmalonic Encephalopathy (ETHE1)

Fabry disease (GLA)
- ❑ 2321 GLA sequencing
- ❑ 906 GLA deletion/duplication testing if sequencing is negative, females

❑ 2843 Fumarate hydratase deficiency (FH) (see also hereditary leiomyomatosis)

❑ 499 Galactokinase Deficiency (GALK1)

❑ 349E Galactosemia / Galactosyltransferase deficiency (GALT) sequencing and deletion/duplication testing

❑ 399 Glutaric aciduria type I (GCDH)

Glutaric aciduria II / Multiple acyl-CoA dehydrogenase deficiency (MADD)
- ❑ 280 ETFDH ❑ 279 ETFB ❑ 278 ETFA
- ❑ 457 ETFDH / ETFB / ETFA tiered testing

Glycerol kinase Deficiency (GK)
- ❑ 438 GK sequencing ❑ 906 GK Exon-level deletion testing

❑ 287 Glycogen storage disease II (Pompe disease) (GAA)

❑ 230 GTP cyclohydrolase I deficiency (GCH1)† (see dopa-responsive dystonia)

HMG CoA lyase deficiency (HMGCL)
- ❑ 3211 HMGCL full gene sequencing
- ❑ 3212 HMGCL sequence exon 2 only (Saudi/Spanish mutation)
- ❑ 3213 Sequence rest of HMGCL gene, (if 3212 negative)

❑ 320 Holocarboxylase synthetase deficiency (HLCS)

❑ 331 Homocystinuria (CBS)

❑ 351 Isobutyryl CoA dehydrogenase deficiency (ACAD8)

Isovaleric acidemia (IVD)
- ❑ 3191 Full sequencing
- ❑ 3192 Sequence exon 9 only (includes common A282V mutation)
- ❑ 3193 Rest of IVD (if 3192 negative)

❑ 507 Krabbe disease (GALC)

LCHAD/trifunctional protein deficiency (HADHA/HADHA and HADHB)
- ❑ 2711 HADHA Tier 1 (common mutation; c.1528G>C)
- ❑ Reflex testing: HADHA (full), HADHB if necessary: 2712, 272
- ❑ 2712 HADHA Full sequencing ❑ 272 HADHB Full sequencing

Lowe syndrome (OCRL)
- ❑ 335 Lowe syndrome, OCRL full sequencing
- ❑ 906 OCRL deletion/duplication testing if sequencing negative, females only

❑ 404 Malonyl-CoA decarboxylase deficiency (MLYCD)

Maple Syrup Urine Disease (MSUD)
- ❑ 4881 BCKDHA ❑ 4882 BCKDHB ❑ 4883 DBT
- ❑ 488 BCKDHA/ BCKDHB/ DBT All now

MCAD deficiency (ACADM)
- ❑ 2682 Full gene sequencing NOW
- ❑ 2681 Sequence exon 11 only (includes common K329E mutation)
- ❑ 2683 Rest of ACADM
- ❑ 456 T1211 (common Saudi Arabian mutation)

Specimen Requirements ALL tests offered by GeneDx can be performed with whole blood specimen. As an alternative to blood, buccal specimen collection kits (supplied by GeneDx) can be used for many tests. Some exceptions are tests marked with "†" and any deletion/duplication, microarray, and non-conventional sequencing tests.

Please check appropriate boxes and fax only the sheets necessary

TEST CODE TEST NAME

❑ 473 Methionine adenosyltransferase I/III deficiency (MAT1A)

2-Methyl-3-hydroxybutyryl-CoA dehydrogenase deficiency (HSD17B10)
- ❑ 463 HSD17B10 sequencing
- ❑ 906 HSD17B10 deletion/duplication testing if sequencing is negative, females

3-Methylcrotonyl CoA carboxylase deficiency
- ❑ 2881 Tier 1: MCCC2 ❑ 2882 Tier 2: MCCC1, if necessary
- ❑ 2883 MCCC1, MCCC2 both NOW

❑ 501 3-Methylglutaconic aciduria type I (AUH)

Methylmalonic acidemia (MUT, MMAA, MMAB)
- ❑ 2751 Reflex testing: MUT, MMAA, MMAB, if necessary
- ❑ 2752 MUT full sequencing ❑ 276 MMAA ❑ 277 MMAB
- ❑ MUT, MMAA, MMAB all NOW: 2752, 276, 277
- ❑ 2753 MUT sequence exon 2 only (Hispanic mutations)
- ❑ 2754 MUT, rest of gene, after 2753, if necessary

❑ 2431 Tier 1 Mucolipidosis type IV (MCOLN1) common Ashkenazi mutations only

❑ 2432 Tier 2 Mucolipidosis type IV (MCOLN1) sequence analysis

❑ 478 N-acetylglutamate synthase deficiency (NAGS)

Niemann-Pick disease (NPD)
- ❑ 2631 NPD type A/B, SMPD1 full gene sequencing
- ❑ 2632 NPD type A/B (SMPD1) Ashkenazi Jewish mutations
- ❑ 246 NPD type C1 (NPC1) ❑ 247 NPD type C2 (NPC2/HE1)
- ❑ 355 NPD type C reflex testing (NPC1, NPC2 if necessary)

Ornithine transcarbamylase deficiency (OTC)
- ❑ 313 OTC sequencing (males)
- ❑ 313E OTC sequencing and deletion/duplication testing (females)

❑ 273 Phenylalanine hydroxylase (PAH)

❑ 287 Pompe disease/glycogen storage disease type II (GAA)

Propionic acidemia
- ❑ 2901 Tier 1: PCCB ❑ 2902 Tier 2: PCCA, if necessary
- ❑ 2903 PCCA, PCCB both NOW

❑ 365 Primary/systemic carnitine deficiency (SLC22A5)

Pyruvate Dehydrogenase E1-Alpha Deficiency (PDHA1)
- ❑ 461 PDHA1 sequencing
- ❑ 906 PDHA1 deletion/duplication testing if sequencing is negative, females

❑ 462 Pyruvate Dehydrogenase E1-Beta Deficiency (PDHB)

Short/branched chain acyl-CoA dehydrogenase deficiency (ACADSB)
- ❑ Full Sequencing
- ❑ 529 M389V (common Hmong mutation)

❑ 269 Short-chain acyl-CoA dehydrogenase (SCAD) deficiency (ACADS)

Smith-Lemli-Opitz syndrome (DHCR7)
- ❑ 2502 DHCR7 sequencing
- ❑ 2503 Prenatal DHCR7 test based on ultrasound abnormalities

Tyrosinemia type I (FAH)
- ❑ 3661 FAH full sequencing ❑ 3662 Sequencing exon 12 only
- ❑ 3663 FAH rest of the gene (if 3662 negative)

❑ 494 Tyrosinemia Type II (TAT)

❑ 495 Tyrosinemia Type III (HPD)

❑ 270 Very long chain acyl-CoA dehydrogenase (VLCAD) deficiency (ACADVL)

Mitochondrial disorders – please use separate submission form

❑ 394 POLG related disorders (POLG)

Noonan, LEOPARD, cardiofaciocutaneous, and Costello syndromes and related disorders

❑ 534 Comprehensive resequencing array for Noonan syndrome and related disorders (PTPN11, SOS1, RAF1, KRAS, BRAF, MAP2K1/MAP2K2, HRAS, SHOC2, CBL, NRAS)

Individual gene testing -
- ❑ 191 Entire HRAS gene
- ❑ 192 Entire PTPN11 gene
- ❑ 389 SHOC2 (S2G mutation only)

Noonan syndrome – prenatal testing based on ultrasound findings
- ❑ 357 Comprehensive Noonan syndrome prenatal panel Genes: PTPN11, SOS1, RAF1, KRAS, BRAF, MAP2K1/MAP2K2, HRAS, SHOC2 (S2G mutation)

Neurodevelopmental intellectual disability disorders

Angelman/Angelman-Like Syndrome
- ❑ 374 UBE3A Sequencing
- ❑ 375 SLC9A6 Sequencing

TEST CODE TEST NAME

Autism/macrocephaly syndrome (PTEN)
- ❑ 195 PTEN sequencing and deletion/duplication testing

Coffin-Lowry syndrome (RSK2)
- ❑ 1101RSK2 Tier 1 sequencing
- ❑ 1102 RSK2 Tier 2 sequencing, if Tier 1 negative
- ❑ 906 RSK2 del/dup testing if sequencing negative, females only
- ❑ 1104 Full RSK2 gene sequencing NOW

Rett syndrome / Atypical Rett syndrome (MECP2)
- ❑ 3041 MECP2 sequencing
- ❑ 906 MECP2 deletion/duplication testing if sequencing is negative

Rubinstein-Taybi syndrome (CREBBP) †
- ❑ 2921 CREBBP Tier 1 mutation hotspots and del/dup testing
- ❑ 2922 CREBBP Rest of gene sequencing if Tier 1 negative

Smith-Magenis syndrome (RAI1)
- ❑ 2511 Sequencing and intragenic deletion/duplication testing

X-linked infantile spasm / Atypical Rett (CDKL5/STK9)
- ❑ 3051 CDKL5 sequencing
- ❑ 906 CDKL5 deletion/duplication testing if sequencing is negative

Other hereditary skin disorders

❑ 197 Birt-Hogg-Dubé syndrome (FLCN)

Carney complex (PRKAR1A)
- ❑ 198 PRKAR1A sequencing
- ❑ 906 PRKAR1deletion/duplication testing if sequencing is negative

Cowden Syndrome (PTEN) † (see also BRRS)
- ❑ 195 PTEN sequencing and deletion/duplication testing

❑ 201 Darier Disease (ATP2A2)

Familial cutaneous malignant melanoma
- ❑ 2021 CDKN2A/p16 and CDK4 (exon 2)
- ❑ 2022 CDKN2A/p16 only

Gorlin Syndrome (PTCH) †
- ❑ 205 Sequencing and deletion/duplication testing

❑ 206 Hailey-Hailey disease (ATP2C1)

Hereditary leiomyomatosis and renal cell carcinoma (FH)
- ❑ 2841 FH Tier 1 sequencing ❑ 2842 FH Tier 2 sequencing
- ❑ 906 FH deletion/duplication testing if sequencing is negative

Incontinentia pigmenti (IKBKG/NEMO)
- ❑ 2861 Tier 1: Common deletion assay for females only
- ❑ 2862 Tier 2: IKBKG full gene sequencing if tier 1 negative

Peutz-Jeghers syndrome (STK11)
- ❑ 2071 Sequencing and deletion/duplication testing

Pseudoxanthoma elasticum (PXE; ABCC6)
- ❑ 2641 Tier 1: Common mutations
- ❑ 2642 Tier 2: Full gene sequencing if T1 negative

❑ 130 Syndromic PPK (incl. Vohwinkel syndr.) (GJB2, connexin 26)

Other keratin disorders

❑ 208 Epidermolytic PPK of Vörner (KRT9 hotspots)

Pachyonychia congenita
- ❑ 2091 KRT16, KRT6a hotspots (PC1)
- ❑ 2092 KRT17, KRT6b hotspots (PC2)

❑ 2111 Steatocystoma multiplex (KRT17 hotspots)

❑ 2131 White sponge nevus (KRT4, KRT13 hotspots)

❑ 266 Dowling-Degos disease (KRT5)

❑ 267 Naegeli-Franceschetti-Jadassohn syndrome (NFJS; KRT14)

Non-epidermolytic PPK (Unna-Thost)
- ❑ 2122 KRT1 full gene sequencing
- ❑ 2121 KRT16 mutation hotspots ❑ 2123 KRT16 full gene sequencing

❑ 265 Transgredient non-epidermolytic PPK (Greither) (KRT5)

Periodic fever syndromes

❑ 367 Comprehensive panel for Periodic Fever Syndromes: Familial Hibernian Fever/TRAPS; Familial Mediterranean Fever; Hyper-IgD Syndrome; Muckle Wells/Familial Cold Urticaria, NOMID; Cyclic neutropenia; PAPA Syndrome; Majeed syndrome (MEFV, TNFRSF1A, MVK, NLRP3 (CIAS1), ELANE (ELA2), PSTPIP1, and LPIN2)

❑ 400 Rest of fever panel if 2 or more genes of the Periodic Fever Panel have been previously tested

❑ 214 Familial Mediterranean fever (MEFV) Exons 2,3 and 10 only

❑ 215 Familial Hibernian fever/ TRAPS (TNFRSF1A) Exons 2-5 only

❑ 216 Hyper-IgD Syndrome (MVK) Exons 8 and 10 only

❑ 217 Muckle-Wells/familial cold urticaria/NOMID (CIAS1) Exon 3 only

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TEST CODE TEST NAME

Pyogenic sterile arthritis, pyoderma gangrenosum, acne (PAPA) (PSTPIP1)
- ❑ 2101 Tier 1 (Exons 10,11) ❑ 2102 Tier 2 (rest), if Tier 1 negative

Pheochromocytoma and related cancer syndromes

von Hippel-Lindau syndrome (VHL)
- ❑ 332 VHL sequencing and deletion/duplication testing

Hereditary paraganglioma-pheochromocytoma syndrome
- ❑ 322 SDHB sequencing
- ❑ 906 SDHB/C/D deletion/duplication testing
- ❑ 324 SDHD sequencing
- ❑ 323 SDHC sequencing

❑ 454 SDHAF2 targeted testing (G78R mutation only)

Sex differentiation disorders

❑ 339 Adrenal hyperplasia, POR deficiency (POR)
❑ 469 5-alpha reductase deficiency (SRD5A2)

Androgen Insensitivity Syndrome (AR) †
- ❑ 220 AR sequencing
- ❑ 2201 Prenatal AR test based on ultrasound abnormalities

❑ 340 Aromatase deficiency (CYP19A1)

Campomelic dysplasia (SOX9)
- ❑ 338 SOX9 sequencing
- ❑ 906 SOX9 deletion/duplication testing if sequencing is negative
- ❑ 3383 Prenatal SOX9 test based on ultrasound abnormalities

❑ 341 XY gonadal dysgenesis (NR5A1/SF-1 sequencing)
❑ 259 XY gonadal dysgenesis (SRY sequencing)
❑ 409 Prenatal SRY test based on ultrasound abnormalities
❑ 422 XY gonadal dysgenesis (DHH sequencing)
❑ 906 XY gonadal dysgenesis (NR0B1/DAX1 testing for gene duplication)

Other genetic disorders

Aicardi-Goutieres Syndrome (TREX1, RNASEH2A, RNASEH2B, RNASEH2C)
- ❑ 4701 Tier 1:TREX1, RNASEH2B exons 2, 6-7
- ❑ 4702 Tier 2: RNASEH2C full gene, RNASEH2A full gene, RNASEH2B remaining exons
- ❑ 4703 RNASEH2C Pakistani founder mutation

❑ 218 Alexander disease (GFAP)
❑ 219 Allgrove (Triple-A) syndrome (AAAS)

Alport syndrome (COL4A5)
- ❑ 2811 COL4A5 sequencing
- ❑ 906 COL4A5 del/dup testing if sequencing negative

Bannayan-Riley-Ruvalcaba syndrome (PTEN) † (see also Cowden syn.)
- ❑ 195 PTEN sequencing and deletion/duplication testing

❑ 372 Bloom Syndrome (BLM)
❑ 317 Branchiootic syndrome 3 (SIX1)

Branchiootorenal syndrome 3 (EYA1)
- ❑ 315 EYA1 sequencing and deletion/duplication testing

❑ 225 Cartilage-hair hypoplasia and associated disorders (RMRP)

CHARGE syndrome (CHD7)
- ❑ 2261 CHD7 sequencing
- ❑ 906 CHD7 deletion/duplication testing if sequencing is negative
- ❑ 2262 Prenatal CHD7 test based on ultrasound abnormalities

Cerebral Cavernous Malformations (CCM) †
- ❑ 4181 KRIT1 Tier 1 sequencing (exons 14, 16, and 18)
- ❑ 4182 KRIT1 Tier 2 sequencing (rest of KRIT1) + deletion/duplication testing (KRIT1/CCM2/PDCD10)
- ❑ 419 CCM2 sequencing
- ❑ 420 PDCD10 sequencing
- ❑ 906 KRIT1/CCM2/PDCD10 deletion/duplication testing ONLY

Chondrodysplasia punctata, X-linked (ARSE)
- ❑ 282 ARSE sequencing (males)
- ❑ 282E ARSE sequencing and deletion/duplication testing (females)

❑ 413 Chuvash Polycythemia (VHL)
❑ 227 Cohen syndrome (COH1) ❑ 2271 Finnish mutation only

Craniofrontonasal dysplasia (EFNB1)
- ❑ 3251 EFNB1 sequencing
- ❑ 906 EFNB1 del/dup testing if sequencing negative, females only

❑ 229 Dent disease, X-linked recessive nephrolithiasis (CLCN5)
❑ 906 CLCN5 del/dup testing if sequencing negative, females only

Dopa-responsive dystonia (GCH1, TH) †
- ❑ 230 GCH1 sequencing
- ❑ 906 GCH1 deletion/duplication testing if sequencing is negative
- ❑ 359 Infantile Parkinsonism (TH deficiency) - TH sequencing

Feingold syndrome (MYCN)
- ❑ 260 MYCN sequencing
- ❑ 906 MYCN deletion/duplication testing if sequencing is negative

Grieg Cephalopolysyndactyly syndrome
- ❑ 472 GLI3 sequence (exons 1-15) and deletion/duplication analysis

Hereditary angioedema
- ❑ 2341 Type I/II C1NH sequencing and deletion/duplication testing
- ❑ 388 Type III F12 sequencing of exon 9 (Thr328 mutation)

Hermansky-Pudlak syndrome (HPS1 and HPS3)
- ❑ 188 HPS1 and HPS3 Puerto Rican mutations
- ❑ 189 HPS3 Ashkenazi splice mutation

Hirschsprung disease (RET)
- ❑ 2351 RET sequencing of select exons
- ❑ 2352 RET sequencing of remaining exons if select exons negative
- ❑ 906 RET deletion/duplication testing if sequencing is negative

Holoprosencephaly (SHH, ZIC2, SIX3, TGIF) †
- ❑ 2371 Sequencing and deletion/duplication testing
- ❑ 2373 Prenatal test based on ultrasound abnormalities

❑ 238 Inclusion body myopathy (GNE; M712T only)
❑ 239 Insensitivity to pain and anhidrosis (NTRK1)

Kallmann syndrome:
- ❑ 2401 KAL1 gene sequencing
- ❑ 906 KAL1 del/dup testing if sequencing is negative, females only
- ❑ 2402 FGFR1 gene

Nemaline myopathy, autosomal recessive
- ❑ 244 Nemaline myopathy (ACTA1) †
- ❑ 245 Nemaline myopathy (NEB; Askenazi Jewish mutation)

Oral-facial-digital syndrome type 1 (OFD1, aka CXORF5)
- ❑ 3641 Tier 1 OFD1 sequencing
- ❑ 3642 Tier 2 OFD1 sequencing
- ❑ 906 OFD1 deletion/duplication testing if sequencing is negative

Pallister Hall Syndrome
- ❑ 4711 Tier 1 GLI3 sequence analysis of exons 13-15
- ❑ 4712 Tier 2 GLI3 sequence analysis of remaining exons (1-12) and del/dup analysis

Renal-Coloboma Syndrome / Papillorenal Syndrome
- ❑ 5211 PAX2 Tier 1 sequencing
- ❑ 5212 PAX2 Tier 2 sequencing (rest of PAX2)
- ❑ 5213 PAX2 full gene sequencing
- ❑ 906 PAX2 deletion/duplication testing

Simpson-Golabi-Behmel Syndrome (SGBS)
- ❑ 415 GPC3 sequencing (males)
- ❑ 415E GPC3 sequencing and deletion/duplication testing (females)

Sotos Syndrome
- ❑ 406 NSD1 sequencing and deletion/duplication testing

Spinal muscular atrophy with respiratory distress, type 1 (IGHMBP2)
- ❑ 342 IGHMBP2 sequencing

❑ 401 Supravalvular aortic stenosis / autosomal dominat cutis laxa (ELN)
❑ 363 Transthyretin amyloidosis/familial amyloid cardiomyopathy (TTR)

Usher syndrome type 2
- ❑ 4051 Tier 1: USH2A 2299delG mutation only
- ❑ 4052 Tier 2: USH2A sequencing and deletion/duplication testing

Van der Woude syndrome (IRF6)
- ❑ 253 IRF6 sequencing

Velocardiofacial syndrome / DiGeorge syndrome (TBX1)
- ❑ 358 TBX1 sequencing

X-linked Adrenal Hypoplasia Congenita (AHC)
- ❑ 416 NR0B1 sequencing

X-linked hydrocephalus, X--linked spastic paraplegia, MASA, CRASH syndrome (L1CAM)
- ❑ 2551 Sequencing (male)
- ❑ 2551E Sequencing and deletion/duplication testing (female)
- ❑ 2553 Prenatal L1CAM test based on ultrasound abnormalities (male)
- ❑ 2553E Prenatal L1CAM test based on ultrasound abnormalities (female)

Payment Options

1. Institutional Billing Information:

PO#/Department Code

Hospital/Lab Name

Contact Name

Address

City State Zip Code

Phone Fax

INSTITUTIONAL BILLING ADDRESS STAMP

2. Payment by credit card

The full amount of the test fee is charged at the time of sample submission.

Name as it appears on card

Billing address

City State Zip Code

Phone

❒ Mastercard ❒ Visa ❒ Discover ❒ American Express

Account Number

Expiration date 3/4 Digit Security Code

Please bill my credit card in the amount of $_____ for diagnostic laboratory tests performed by GeneDx, Inc.

Signature (Required) Date

3. Payment by check or money order:

Minimum of 75% of the cost of the test is required at the time of sample submission, with the remainder of the fee billed at the time of test completion.*

Check or money order enclosed in the amount of $_____.

**** For patients from outside the United States, 100% of the fee is due at the time of sample submission***

4. Insurance Billing:
(Must also complete Section 2, credit card info)

GeneDx cannot bill Medicare. GeneDx is not a particpating member with any Medicaid/MediCal program.

GeneDx does not bill Insurance Companies directly unless all of the following is submitted:

- Credit card information (complete part 2) to which any outstanding balance may be billed;
- An authorization number or letter of agreement from the insurance company.
  - The letter of agreement should be directed to GeneDx
  - detail the reimbursement rate
  - the name of the department or individual to whom the bill will be sent (including address, phone and fax numbers)
  - the patient's name and policy number.
- Copy of both sides of the insurance card.
- ICD9 codes (to be provided by physician) _____

I UNDERSTAND THAT I AM RESPONSIBLE IN ALL CASES FOR ALL FEES NOT COVERED BY INSURANCE.

Signature (Required)

Note

IF YOU plan to apply on your own to your insurance carrier for reimbursement of your expenses for this test, the following information may be helpful in the case that GeneDx is requested by the carrier to prepare supporting documentation for you to use in your insurance claim:

Insurance Carrier
Is this a Blue Cross/Blue Shield Plan? ❒ YES ❒ NO

Subscriber Name
Is this a Medicaid plan? ❒ YES ❒ NO

Subscriber DOB